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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,615	06/26/2001	Gregory Plowman	038602-1214	8543

7590 03/04/2004

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EXAMINER	
BORIN, MICHAEL L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,615	PLOWMAN ET AL.	
	Examiner	Art Unit	
	Michael Borin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-12 and 14-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-30 are currently pending.

Response to restriction requirement filed 12/03/2003 is acknowledged. Applicant elected, with traverse, Group V and sequence SEQ ID No. 73. Applicant argues, first, that PTO's policy is to examine "up to ten" nucleotide sequences. The elected subject matter, however, is use of peptides, not nucleotides. Further, as cited in the restriction requirement, MPEP 803.04 states that:

> Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141

Applicant also asserts that there are certain common structural features among the claimed products; however, such core structures are not identified as claimed. Additionally, applicant argues that search of a polypeptide together with polynucleotide encoding the peptide would not be burdensome. First, polypeptides and polynucleotide are separately classified which would require separate searches of patent literature. Second, polypeptides have been most commonly, albeit not always, separately characterized and published in the biochemical literature, thus significantly adding to the search burden if examiner together, as compared to being searched separately. Second, the elected invention is not drawn to a product itself, but to a polypeptide-

based screening assay, thus making searches different with the group directed to a polynucleotide product.

The restriction requirements still deemed proper and is therefore made FINAL. Claims 1-12, 14-30 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups. Cancellation of claims 1-12, 14-30 and amendment of claim 13 to read on elected SEQ ID No. 73 are requested.

Priority

2. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional applications upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for the elected SEQ ID NOs. No CRF was filed with the provisional applications to which priority is claimed. It is possible that the provisional application recites a sequence which is the same as instant SEQ ID NOs, but in the absence of a CRF for the application, the examiner has no way of determining whether any sequence recited in the provisional application is identical to instant SEQ ID Nos. Given the large number of sequences recited in the provisional application, and given the size of SEQ ID Nos. in the present case and each of the sequences recited in the provisional application, it would require undue effort on the part of the examiner to determine which, if any, of the sequences recited in the

provisional application is identical to instant SEQ ID Nos. Applicant is requested to point to the specific SEQ ID number(s) in any or each of the provisional applications that correspond to instant SEQ ID NO. 73, and to the specific page and line, or to the specific page and Table designation where the corresponding SEQ ID NO. Is taught. In the absence of any indication of such correspondence and/or an alignment showing identity between SEQ ID NO, priority is not granted to the provisional application, and the instant application is granted priority only to its filing date.

Specification

3. Specification is objected for the following reasons:

A. p. 5, line 25, addresses "nucleic acid molecule having amino acid sequence...". Nucleic acids do not have amino acid sequence.

B. In describing protease polypeptides, pages 163-193, specification provides their comparison with sequences in database NRAA. It is not clear what abbreviation NRAA stands for - it might be, for example, database of National Renal Administration Administrators, or database of *Porphyromonas gingivalis* genome project (see attached). The issue is essential for identification of the identity of the claimed polypeptide (see utility rejection below).

C. The specification is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, for example, pages 123, 129, 132. See MPEP § 608.01(b).

Information Disclosure Statement

4. Applicants' Information Disclosure Statement filed 06/07/2002 has been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Title, Abstract

5. The title and abstract of the invention are not descriptive. The title and abstract do not reflect the elected invention. A new title and abstract are required which are clearly indicative of the invention to which the elected claims are directed.

Sequence Listing

6. The Sequence Listing was approved by STIC for matters of form.

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear which method step results in the claim's objective of identifying a substtabnce that modifies activity of protease polypeptide. There is no "identifying" method step claimed, and it is no what reklationship, if any, to the claim's objective has monitoring of various changes in the cell features recited in step (c).

Further, the meaning of the term "substantially identical" in regard to SEQ ID No. 73 is not clear. It is a relative term, but no standard of reference has been provided with which to determine whether a particular sequence is "substantially identical" or not. Accordingly, it is not possible to determine what sequences are embraced within the scope of the claim.

Claim Rejections - 35 U.S.C. § 101/ 112-1

8. Claim 13 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claim is drawn to method of identifying a modulator of polypeptide SEQ ID No. 73 by expresssing the polypeptide in a cell, adding a test compound and monitoring changes in cell properties.

Since neither a modulator of polypeptide SEQ ID No. 73 is disclosed, nor a utility for such particular modulator is addressed, the utility of the method as claimed relies on the utility of polypeptide SEQ ID No. 73 itself. Specification does not disclose any utility for polypeptide SEQ ID No. 73 itself but provides result of database search identifying the polypeptide as an ubiquitin specific protease (see p. 170, last paragraph). However, results of such database analysis are not acceptable because 1) it is not clear what kind of database was used for comparing (see objection to specification above), and 2) when the accession number NP_115971.1 (which has, according to specification, 99% sequence similarity of SEQ ID 73) was searched in NCBI database, it yielded a sequence of a protein which, although indeed being a ubiquitin specific protease, does not have any sequence similarity with SEQ ID No. 73 (see printout attached). As for assertions of presence of certain domains in SEQ ID No. 73, such as protease domain, calcium binding domains, the presence of a given motif within a protein sequence does not establish preponderence of evidence that the protein would, in fact, have the function associated with the motif. Therefore,

Examiner concludes that there is no specific or substantial utility demonstrated for either polypeptide SEQ ID No. 73 or a modulator thereof.

Much less there would be utility demonstrated for a sequence which is, as addressed by the claim, is "substantially identical" to sequence of SEQ ID No. 73) Identifying a polypeptide as having a limited homology to the claimed polypeptides does not indicate what function it might have. Assignment to a prior art family of polypeptides is generally insufficient to meet the utility requirement unless such assignment would allow the artisan to assign a specific and substantial use to the new member of the polypeptide family. Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) disclose that the skilled artisan is well aware that assigning functional activities for any particular polypeptide or polypeptide family based upon sequence homology is inaccurate, in part because of the multifunctional nature of polypeptides (see, e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two polypeptides, only experimental research can confirm the artisan's best guess as to the function of the structurally related polypeptide (see in particular "Abstract" and Box 2). Thus, the homology-based assignment of the claimed polypeptide does not appear to provide evidence of a specific and substantial utility based on the knowledge of the skilled artisan and the data presented in the instant specification.

10. Claim 13 is also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility, one skilled in the art would not know how use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph (written description).

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim addresses polypeptide comprising SEQ ID No. 73 as a protease. Specification provides result of database search identifying the polypeptide as an ubiquitin specific protease (see p. 170, last paragraph). However, results of such database analysis are not acceptable because 1) it is not clear what kind of database was used for comparing (see objection to

specification above), and 2) when the accession number NP_115971.1 (which has, according to specification, 99% sequence similarity of SEQ ID 73) was searched in NCBI database, it yielded a sequence of a protein which, although indeed being a ubiquitin specific protease, does not have any sequence similarity with SEQ ID No. 73 (see printout attached). Therefore, there is no sufficient evidence of record demonstrating that the polypeptide comprising SEQ ID No. 73 is a protease, ubiquitin specific protease in particular.

Conclusion.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. Dr. Borin can normally be reached between the hours of 8:30 A.M. to 5:00 P.M. EST Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0549.

MICHAEL BORIN, PH.D
PRIMARY EXAMINER